LUD 5330.1-CEL/NDH

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s)	:	Rainer Zimmermann, et al.
Serial No.	:	08/619,280
Filed	:	March 18, 1996
For	:	ISOLATED DIMERIC FIBROBLAST ACTIVATION PROTEIN ALPHA, AND USES THEREOF
Art Unit	:	1818
Examiner	:	M. Allen

Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

DECLARATION

Norman D. Hanson hereby declares as follows:

1. I am the attorney in charge of the subject application, and its parent application, Serial No. 08/230,491, filed April 20, 1994.

2. The parent application is incorporated by reference at page 2, lines 1-4 of the current application.

3. In the course of prosecution of the parent application, I submitted an amendment on November 13, 1995. This amendment

included sequence information. This amendment was received and entered in the parent application

4. When the subject continuation-in-part application was filed, I submitted a proper request, under 37 C.F.R. § 1.821(e) to have sequence information transferred from the parent application. I properly referred to the date of the sequence submission, and I properly included a paper copy of the material. I also expressly stated that no new matter was presented.

5. It is not clear to me why this declaration was not acceptable. There is no reason for this on the record.

6. Nonetheless, I hereby state that the material submitted on March 18, 1996 is identical to material submitted in the parent application on November 13, 1995. The paper copy submitted on March 18, 1996 was prepared from the same computer readable form of sequence information sent to the USPTO on November 13, 1995. I compared the paper copy submitted on November 15, 1995 to that submitted on March 18, 1996 and, to the best of my knowledge, these are identical, and no new matter is presented.

7. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the

like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

August 20, 1997
Date

Norman D. Hanson
Reg. No. 30,946

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s)	:	Wolfgang J. Rettig, et al.
Serial No.	:	08/230,491
Filed	:	April 20, 1994
For	:	ISOLATED NUCLEIC ACID MOLECULE CODING FOR FIBROBLAST ACTIVATION PROTEIN ALPHA AND USES THEREOF
Art Unit	:	1812
Examiner	:	M. Allen

Hon. Commissioner of Patents
and Trademarks
Washington, D.C. 20231

DECLARATION

The undersigned hereby declare as follows:

1. We are the inventors of the invention described and claimed in the above-referenced patent application. We are fully familiar with its content.

2. We wish to bring the Examiner's attention to errors in the nucleotide sequence and the amino acid sequence of this application.

3. Specifically, three nucleotides need to be added, as follows:

With reference to SEQ ID NO: 1, a G has to be added between bases 2084-2085, 2085-2086, and 2216-2217. This results in a need to change amino acids 626-668 in figure 3. For convenience, copies of original figure 3 and replacement figure 3 are attached, with pertinent material boxed.

4. We became aware of this error after we had isolated and sequenced the murine FAPα gene. We found a very high degree of homology with the human sequence (over 95%), except for the stretch corresponding to amino acids 626-668.

5. As a result, we resequenced the clone described in the application, i.e., pFAP 38, using the methodologies described in this application. It was at this point that we found the omitted bases.

6. We would note that the sequencing was carried out using Sanger et al., Proc. Natl. Acad. Sci. USA 74: 5463-5467 (1979), noted at page 11 of the patent application. It is well known that the Sanger methodology sometimes does not identify adjacent "Gs" in a nucleotide sequence, and "reads" 2 G moieties as a single moiety. Exemplary are the attached materials, i.e., Sambrook & Maniatis, Molecular Cloning, A Laboratory Manual

(CSH, 1989), p. 13.10; Mizusawa, et al., Nucl. Acids Res. 14(3): 1319-1324 (1986); Seela, U.S. Patent No. 4,804,748 (February 14, 1989). That is indeed what happened here.

7. The error in the sequences was inadvertent, and no deceptive intent is involved. Any inconvenience to the PTO is regretted.

8. As a result of the need to correct the sequences, additional materials in the application must be changed at page 12, lines 8, 9, 12, 13, 22, 23 and page 13, lines 7 and 8.

9. We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may

jeopardize the validity of the application or any patent issued thereon.

7/27/95
Date

Wolfgang Hartig

7/27/95
Date

Matthew Scanlan

7/27/95
Date

Pilar Gafin-Chesa

RIGINAL
IGURE

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FAP      1  MKTWVKVV J*ATSAVLALLVMCIVLRPSRVH E- TMRALTLKDILN  49
CD26     1  ---PW LL-LLGAA-LVTIITVPV--LNKGTDDATADSRKTY--T-Y-K  50

FAP     50  GTFSYKTFFPNWISGQEYLHQSADNNIVLYNIETGQSYTILSNRTMKSV*  98
CD26    51  N-YRL-LYSLR---DH---YKQ*E---LVF-A-Y-N-SVF-E-S-FDEFG  99

FAP     99  *NASNYGLSPDRQFVYLESDYSKLWRYSYTATYYIYDLSNGEFVRGNELP 147
CD26   100  HSIND-SI---G--IL--YN-V-Q--K----S-D----NKRQLITEERI- 149

                                                    fap-1
FAP    148  RPIQYLCWSPVGSKLAYVYQNNIYLKQRPGDPPFQITFNGRENKIFNGIP 197
CD26   150  NNT-WVT-----H-----WN-D--V-IE-NL-SYR--WT-K-DI-Y---T 199

                  fap-2
FAP    198  DWVYEEEMLPTKYALWWSPNGKFLAYAEFNDKDIPVIAYSYYGDE**QYP 245
CD26   200  -------VFSAYS--------T-----Q---TEV-L-E--F-S--SL--- 249

FAP    246  RTINIPYPKAGAKNPVVRIFIIDT***TYPAYVGPQEVPVPAMIASSDYY 292
CD26   250  K-VRV-------V--T-KF-VVN-DSLSSVTNATSIQITA--SMLIG-H- 299

FAP    293  FSWLTWVTDERVCLQWLKRVQNVSVLSICDFREDWQTWDCPKTQEHIEES 342
CD26   300  LCDV--A-Q--IS----R-I--Y--MD---YD-SSGR-N-LVARQ---M- 349

FAP    343  RTGWAGGFFVSRPVFSYDAISYYKIFSDKDGYKHIHYIKDTVENAIQITS 392
CD26   350  T---V-R-RP-E-H-TL-GN-F---I-NEE--R--C-FQIDKKDCTF--K 399

FAP    393  GKWEAINIFRVTQDSLFYSSNEFEEYPGRRNIYRISIGSYPPSKKCVTCH 442
CD26   400  -T--V-G-EAL-S-Y-Y-I---YKGM--G--L-K-QLSD-T*KVT-LS-E 448

FAP    443  LRKERCQYYTASFSDYAKYYALVCYGPGIPISTLHDGRTDQEIKILEENK 492
CD26   449  -NP-------SV---KE----Q-R-S---L-LY---SSVN-KGLRV--D-S 498

                  fap-3
FAP    493  ELENALKNIQLPKEEIKKLEVDEITLWYKMILPPQFDRSKKYPLLIQVYG 542
CD26   499  A-DKM-Q-V-M-SKKLDFIILN-TKF--Q-----H--K-------LD--A 548

FAP    543  GPCSQSVRSVFAVNWISYLASKEGMVIALVDGRGTAFQGDKLLYAVYRKL 592
CD26   549  -----KADT--RL--AT----T-NIIV-SF----SGY----IMH-IN-R- 598

FAP    593  GVYEVEDQITAVRKFIEMGFIDEKRIAIWGWSYGGIRFITGPCIWNWSFQM 642
CD26   599  -TF-------E-A-Q-SK---V-N----------GGYVTSMVLGSGSGVFK 648

FAP    643  WYSSGSSLQLGILRVCLHRE*IHGSPNKDDNLEHYKNSTVMARAEYFRNV 691
CD26   649  CGIAVAPVSRWEYYDSVYT-RYM-L-TPE---D--R-----S---N-KQ- 698

FAP    692  DYLLIHGTADDNVHFQNSAQIAKALVNAQVDFQAMWYSDQNHGLSGLSTN 741
CD26   699  E---------------Q----S----DVG--------T-ED--IASSTAH 748

FAP    742  *HLYTHMTHFLKQCFSLSD
CD26   749  Q-I---S--I------P
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produced by [illegible] of ^{35}S, there is little loss of resolution between the gel and the autoradiograph. This allows unambiguous determination of several hundred nucleotides of DNA sequence from a single reaction set. Furthermore, the lower energy of ^{35}S produces less radiolysis, allowing sequencing reactions to be stored for up to 1 week at −20°C without noticeable loss of resolution. Thus, if technical problems arise with a polyacrylamide gel, the sequencing reactions can simply be reanalyzed.

ANALOGS OF dNTPs

Regions of DNA with dyad symmetry (especially those with a high G + C content) can form intrastrand secondary structures that are not fully denatured during electrophoresis. This can cause an anomalous pattern of migration in which adjacent bands of DNA become compressed to the point where they are difficult to read. Compression is entirely dependent on the presence of secondary structures in DNA and cannot be alleviated by changing the type of DNA polymerase used in the sequencing reaction. However, compressed regions of gels can usually be resolved by using a nucleotide analog such as dITP (2′-deoxyinosine-5′-triphosphate) or 7-deaza-dGTP (7-deaza-2′-deoxyguanosine-5′-triphosphate). These analogs pair weakly with conventional bases and are good substrates for DNA polymerases such as the Sequenases and *Taq* DNA polymerase (Gough and Murray 1983; Mizusawa et al. 1986; Innis et al. 1988). Some compressions are not resolved by 7-deaza-dGTP, others (particularly those occurring in GC-rich regions) are not resolved by dITP. If it is necessary to use analogs, try dITP first (see pages 13.74–13.75). This analog, in contrast to 7-deaza-dGTP, does not affect the sharpness of the DNA bands in the sequencing gel. Any compression that is not resolved by either dITP or 7-deaza-dGTP can almost always be cleared up by determining the sequence of both strands of the DNA.

As discussed above, both forms of Sequenase and *Taq* DNA polymerase tolerate nucleotide analogs better than does the Klenow fragment of *E. coli* DNA polymerase I. In addition, the manufacturer claims that Sequenase version 2.0 is superior to the original enzyme when sequencing templates with strong secondary structure. Version 2.0 is more processive than Sequenase, having less tendency to pause, thereby eliminating "ghost" bands. Furthermore, version 2.0 appears to tolerate nucleotide analogs such as dITP better than does the original version.

From: Molecular Cloning 1989
Maniatis